SEQUENCE LISTING

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<110> KYOWA HAKKO KOGYO CO., LTD.
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<120> Substance which inhibits biding of information transfer molecule for 1175-tyrosine phosphorylated KDR/Flk-1 and usages of the same

<130>

<140>

<141>

<150> JP 2000-303694

<151> 2000-10-03

<150> US 60/263, 512

<151> 2001-1-24

<160> 7

<170> PatentIn Ver. 2.1

⟨210⟩ 1

⟨211⟩ 11

<212> PRT

<213> Artificial Sequence

<220>

<221> Phosphorylation

<222> 7

⟨220⟩ .

 $\ensuremath{^{<\!223>}}$ an antigen peptide for human KDR/Flk-1 phosphorylated at 1175-tyrosine corresponding to its residue 1171-1180 and added cysteine residue at the N-terminal

<400> 1

Cys Asp Gly Lys Asp Tyr Ile Val Leu Pro Ile

⟨210⟩ 2

⟨211⟩ 11

<212> PRT

<213> Artificial Sequence

<220>

 $\langle 223 \rangle$ a peptide consisting of the same sequence as SEQ ID NO:1 without phosphorylation

<400> 2

Cys Asp Gly Lys Asp Tyr Ile Val Leu Pro Ile

⟨210⟩ 3

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> a primer for replacing of human KDR/Flk-1 tyrosine residue at position 1175 to phenylalanine.

<400> 3

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27

⟨210⟩ 4

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> a primer for replacing of human KDR/Flk-1 tyrosine residue at position 1214 to phenylalanine.

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cccaaattcc atttcgacaa cacagca

27

⟨210⟩ 5

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> a primer for replacing of human KDR/Flk-1 tyrosine residue at position 801 to phenylalanine.

<400> 5 gacaggette ttgtccateg

20

<210> 6

<211> 20

<212> PRT

<213> Human

<400> 6

Gln Gly Lys Asp Tyr Val Gly Ala Ile Pro Val Asp Leu Lys Arg Arg
1 5 10 15

Leu Asp Ser Ile 20

<210> 7

<211> 1356

<212> PRT

<213> Human

<400> 7

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Thr Arg Ala Ala Ser Val Gly Leu Pro Ser Val Ser Leu Asp Leu Pro 20 25 30

Arg Leu Ser Ile Gln Lys Asp Ile Leu Thr Ile Lys Ala Asn Thr Thr 35 40 45

Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro 50 55 60

Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser 65 70 75 80

Asp	Ģly	L	eu	Phe	Cys 85	Lys	Thr	Leu	Thr	Ile 90	Pro	Lys '	Val		Gly 7 95	Asn
Asp	Thi	- G	ly	Ala 100	Tyr	Lys	Cys	Phe	Tyr 105	Arg	Glu	Thr		Leu 110	Ala	Ser
Val	Ile		yr 15	Val	Tyr	Val	G1n	Asp 120	Tyr	Arg	Ser	Pro	Phe 125	Ile	Ala	Ser
Val	Se 13		lsp	Gln	His	Gly	Val 135		Tyr	Ile	Thr	Glu 140	Asn	Lys	Asn	Lys
Thr 145		1 V	/al	Ile	Pro	Cys 150		ı Gly	Ser	Ile	Ser 155	Asn	Leu	Asn	Val	Ser 160
Leu	ι Су	S	Ala	Are	7 Ty1		Glı	ı Lys	Arg	Phe 170		Pro	Asp	Gly	Asn 175	Arg
Ile	e Se	r	Trp	Ası 180		r Lys	s Lys	s Gly	Phe 185		· Ile	Pro	Ser	Tyr 190	Met	Ile
Sei	r Ty	r	Ala 195		у Ме	t Va	l Ph	e Cys 200		ı Ala	a Lys	s Ile	Asn 205		Glu	Ser
Ту		ln 10	Sei	r Il	e Me	t Ty	r Il 21		l Va	l Vai	l Vai	1 Gly 220		Arg	Ile	Tyr
As; 22		al	Va:	l Le	u Se	r Pr 23		r Hi	s Gl	y Il	e G1: 23:		ı Ser	. Val	Gly	Glu 240
Ly	s L	eu	Va	l Le	u As 24		s Th	r Al	a Ar	g Th 25		u Lei	ı Ası	n Val	Gly 255	Ile
As	рP	he	As	n Tr 26		u Ty	r Pr	o Se	r Se 26		s Hi	s Gli	n Hi:	s Lys 270		s Leu
Va	ıl A	sn	Ar 27		sp Le	eu Ly	s Th	nr G1 . 28		r Gl	y Se	er Gl	u Me 28		s Ly	s Phe
Le		Ser 290		ır L	eu T	hr I		sp G] 95	ly Il	le Th	ur Ar	rg Se 30		p Gl	n Gl	y Leu

Tyr 305	Thr	Cys	Ala	Ala	310	Ser	Gly	Leu 1		315	Lys	Lys	ASN	Ser	320
Phe	Val	Arg	Val	His 325	Glu	Lys	Pro		Val 330	Ala	Phe	Gly	Ser	Gly 335	Met [.]
Glu	Ser	Leu	Val 340	G1u	Ala	Thr		Gly 345	Glu	Arg	Val	Arg	Ile 350	Pro	Ala
Lys	Tyr	Leu 355	Gly	Tyr	Pro	Pro	Pro 360	Glu	Ile	Lys	Trp	Tyr 365	Lys	Asn	Gly
Ile	Pro 370		Glu	Ser	Asn	His 375	Thr	Ile	Lys	Ala	Gly 380	His	Val	Leu	Thr
Ile 385		Glu	Val	Ser	Glu 390	Arg	Asp	Thr	Gly	Asn 395	Tyr	Thr	Val	Ile	Leu 400
Thr	Asn	Pro	Ile	Ser 405	Lys	Glu	Lys	Gln	Ser 410	His	Val	Val	Ser	Leu 415	
Val	Туг	· Val	Pro 420		Gln	Ile	Gly	Glu 425	Lys	Ser	Leu	Ile	Ser 430		Val
Asp	. Sei	7yı 438		1 Туг	Gly	Thr	Thr 440		Thr	Leu	Thr	Cys 445		· Val	Tyr
Ala	450		Pro	Pro	His	His 455		His	Trp	Tyr	Trp 460		Leu	ı Glı	ı Glu
Gl: 465	-	s Ala	a Ası	n Glu	1 Pro 470		Gln	ı Ala	Val	Ser 475		Thr	- Asr	ı Pro	Tyr 480
Pro	о Су	s Gl	u Gl	u Tr 48		g Sei	· Val	l Glu	490		e Glr	Gly	7 Gly	7 Ası 49	n Lys 5
Ile	e Gl	u Va	1 As:		s Asr	n Glr	n Phe	Ala 505		ı Ile	e Glu	ı Gly	y Ly: 510		n Lys

Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr

525

- Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser 530 535 540
- Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln 545 550 555 560
- Pro Thr Glu Gln Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser
 565 570 575
- Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro 580 585 590
- Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr 595 600 605
- Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile 610 615 620
- Leu Ile Met'Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr 625 630 635 640
- Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val 645 650 655
- Arg Gln Leu Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn 660 665 670
- Leu Glu Asn Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys 675 680 685
- Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn 690 695 700
- Glu Thr Leu Val Glu Asp Ser Gly Ile Val Leu Lys Asp Gly Asn Arg 705 710 715 720
- Asn Leu Thr Ile Arg Arg Val Arg Lys Glu Asp Glu Gly Leu Tyr Thr 725 730 735

- Cys Gln Ala Cys Ser Val Leu Gly Cys Ala Lys Val Glu Ala Phe Phe 740 745 750
- Ile Ile Glu Gly Ala Gln Glu Lys Thr Asn Leu Glu Ile Ile Ile Leu 755 760 765
- Val Gly Thr Ala Val Ile Ala Met Phe Phe Trp Leu Leu Leu Val Ile 770 775 780
- Ile Leu Arg Thr Val Lys Arg Ala Asn Gly Gly Glu Leu Lys Thr Gly 785 790 795 800
- Tyr Leu Ser Ile Val Met Asp Pro Asp Glu Leu Pro Leu Asp Glu His 805 810 815
- Cys Glu Arg Leu Pro Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp 820 825 830
- Arg Leu Lys Leu Gly Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val 835 840 845
- Ile Glu Ala Asp Ala Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr 850 855 860
- Val Ala Val Lys Met Leu Lys Glu Gly Ala Thr His Ser Glu His Arg 865 870 875 880
- Ala Leu Met Ser Glu Leu Lys Ile Leu Ile His Ile Gly His His Leu 885 890 895
- Asn Val Val Asn Leu Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu 900 905 910
- Met Val Ile Val Glu Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu 915 920 925
- Arg Ser Lys Arg Asn Glu Phe Val Pro Tyr Lys Thr Lys Gly Ala Arg 930 935 .940
- Phe Arg Gln Gly Lys Asp Tyr Val Gly Ala Ile Pro Val Asp Leu Lys 945 950 955 960

- Arg Arg Leu Asp Ser Ile Thr Ser Ser Gln Ser Ser Ala Ser Ser Gly
 965 970 975
- Phe Val Glu Glu Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Ala Pro 980 985 990
- Glu Asp Leu Tyr Lys Asp Phe Leu Thr Leu Glu His Leu Ile Cys Tyr 995 1000 1005
- Ser Phe Gln Val Ala Lys Gly Met Glu Phe Leu Ala Ser Arg Lys Cys 1010 1015 1020
- Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Lys Asn 1025 1030 1035 1040
- Val Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp 1045 1050 1055
- Pro Asp Tyr Val Arg Lys Gly Asp Ala Arg Leu Pro Leu Lys Trp Met 1060 1065 1070
- Ala Pro Glu Thr Ile Phe Asp Arg Val Tyr Thr Ile Gln Ser Asp Val 1075 1080 1085
- Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser 1090 1095 1100
- Pro Tyr Pro Gly Val Lys Ile Asp Glu Glu Phe Cys Arg Arg Leu Lys 1105 1110 1115 1120
- Glu Gly Thr Arg Met Arg Ala Pro Asp Tyr Thr Thr Pro Glu Met Tyr 1125 1130 1135
- Gln Thr Met Leu Asp Cys Trp His Gly Glu Pro Ser Gln Arg Pro Thr 1140 1145 1150
- Phe Ser Glu Leu Val Glu His Leu Gly Asn Leu Leu Gln Ala Asn Ala 1155 1160 1165
- Gln Gln Asp Gly Lys Asp Tyr Ile Val Leu Pro Ile Ser Glu Thr Leu

1180

- Ser Met Glu Glu Asp Ser Gly Leu Ser Leu Pro Thr Ser Pro Val Ser 1185 1190 1195 1200
- Cys Met Glu Glu Glu Val Cys Asp Pro Lys Phe His Tyr Asp Asn 1205 1210 1215
- Thr Ala Gly Ile Ser Gln Tyr Leu Gln Asn Ser Lys Arg Lys Ser Arg 1220 1225 1230
- Pro Val Ser Val Lys Thr Phe Glu Asp Ile Pro Leu Glu Glu Pro Glu 1235 1240 1245
- Val Lys Val Ile Pro Asp Asp Asn Gln Thr Asp Ser Gly Met Val Leu 1250 1255 1260
- Ala Ser Glu Glu Leu Lys Thr Leu Glu Asp Arg Thr Lys Leu Ser Pro 1265 1270 1275 1280
- Ser Phe Gly Gly Met Val Pro Ser Lys Ser Arg Glu Ser Val Ala Ser 1285 1290 1295
- Glu Gly Ser Asn Gln Thr Ser Gly Tyr Gln Ser Gly Tyr His Ser Asp 1300 1305 1310
- Asp Thr Asp Thr Thr Val Tyr Ser Ser Glu Glu Ala Glu Leu Leu Lys 1315 1320 1325
- Leu Ile Glu Ile Gly Val Gln Thr Gly Ser Thr Ala Gln Ile Leu Gln 1330 1335 1340
- Pro Asp Ser Gly Thr Thr Leu Ser Ser Pro Pro Val 1345 1350 1355